numerous and have been generally inferred from the pedigree, giving rise to the dominant and recessive incidence values (Fine *et al*, 1999).

The new mutation rate for any of the forms of EB has not been calculated; however, a number of sporadic cases of DEB have been analyzed for mutations in the COL7A1 gene and are presumed to result from germline mosaicism (Rouan *et al*, 1998; Hashimoto *et al*, 1999; Lee *et al* 2000). Continued elucidation of the mutations involved in all forms of EB will allow us to further understand the relative numbers of new mutations, and to correlate type of mutation and pattern of inheritance.

The carrier incidence information provided in **Table I** should enable genetics professionals to accurately calculate the risk of recurrence to individual family members based on the family history and provide up-to-date risk estimates that will facilitate accurate counselling of extended families at risk.

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REFERENCES

Chan Y, Anton-Lamprecht I, Yu QC, *et al*: A human keratin 14 "knockout": the absence of K14 leads to severe epidermolysis bullosa simplex and a function for an intermediate filament protein. *Genes Dev* 8:2574–2587, 1994

Christiano A, McGrath J, Uitto J: Influence of the second COL7A1 mutation in determining the phenotypic severity of recessive dystrophic epidermolysis bullosa. *J Invest Dermatol* 106:766–770, 1996

Fine J-D, Bauer EA, McGuire J, Moshell A (eds): *Epidermolysis Bullosa: Clinical, Epidemiologic and Laboratory Advances and the Findings of the National Epidermolysis Bullosa Registry*. Baltimore: The Johns Hopkins University Press, 1999

Fine J-D, Eady RAJ, Bauer EA, *et al*: Revised classification system for inherited epidermolysis bullosa: Report of the Second International Consensus Meeting on diagnosis and classification of epidermolysis bullosa. *J Am Acad Dermatol* 42:1051–1066, 2000

Gardella R, Belletti L, Zoppi N, *et al*: Identification of two splicing mutations in the collagen type VII gene (COL7A1) of a patient affected by the *localisata* variant of recessive dystrophic epidermolysis bullosa. *Am J Hum Genet* 59:292–300, 1996

Hashimoto I, Kon A, Tamai K, Uitto J: Diagnostic dilemma of "sporadic" cases of dystrophic epidermolysis bullosa: a new dominant or mitis recessive mutation? *Exp Dermatol* 8:140–142, 1999

Järvikallio A, Pulkkinen L, Uitto J: Molecular basis of dystrophic epidermolysis bullosa: mutations in the type VII collagen gene (COL7A1). *Hum Mut* 10:338–347, 1997

Jonkman MF, Heeres K, Pas HH, *et al*: Effects of keratin 14 ablation on the clinical and cellular phenotype in a kindred with recessive epidermolysis bullosa simplex. *J Invest Dermatol* 5:764–769, 1996

Lee JY-Y, Li C, Chao S-C, Pulkkinen L, Uitto JA: *De novo* glycine substitution mutation in the collagenous domain of COL7A1 in dominant dystrophic epidermolysis bullosa. *Arch Dermatol Res* 292:159–163, 2000

Pulkkinen L, Uitto J: Mutation analysis and molecular genetics of epidermolysis bullosa. *Matrix Biol* 18:29–42, 1999

Rouan F, Pulkkinen L, Jonkman M, *et al*: Novel and *de novo* glycine substitution mutations in the type VII collagen gene (COL7A1) in dystrophic epidermolysis bullosa: implications for genetic counseling. *J Invest Dermatol* 111:1210–1213, 1998

Rugg EL, McLean WHI, Lane EB, *et al*: A functional "knockout" of human keratin 14. *Genes Dev* 8:2563–2573, 1994

Tamai K, Murai T, Mayama M, *et al*: Recurrent COL7A1 mutations in Japanese patients with dystrophic epidermolysis bullosa: positional effects of premature termination codon mutations on clinical severity. *J Invest Dermatol* 112:991–993, 1999

A Peripheral Blood T Cell Clone is a Prognostic Marker in Mycosis Fungoides

To the Editor:

Dr Muche and colleagues (2000) have raised several criticisms of our recent article (Fraser-Andrews *et al*, 2000). Specifically they question our findings that a peripheral blood T cell clone is an independent prognostic feature in mycosis fungoides ($p = 0.03$ with a hazards ratio of 2.6 after adjusting for age, skin stage, and lymph node stage). Our results are based on multivariate analysis of 66 patients with up to 10 y follow-up and crucially includes analysis of data at diagnosis for the majority of patients. Whilst we acknowledge that further prospective studies of larger numbers with longer follow-up are required, their comment that "the survival or time to progression in stage of the reported mycosis fungoides (MF) patients with or without periphreal blood T cell clonality" is not relevant if data are analyzed from diagnosis. In other words the results at diagnosis give a measure of tumor burden that can then be entered into a multivariate analysis. The reason for the authors differing conclusions is because their study is not based on data at the time of diagnosis and predominanlty consists of patients with T1 and T2 MF and only four patients with T3 stage disease. In addition the follow-up in their study is much shorter than ours. They state that the presence of a peripheral blood T-cell clone fluctuated during the course of the disease in some of their patients, which would be expected and might reflect a partial response to different therapies. Once again this emphasises the importance of analysing data from diagnosis. Inevitably they cannot perform a multivariate analysis on these results and therefore cannot make any conclusoins regarding the prognostic implications.

We agree that the proportion of peripheral blood T cell clones detected will reflect the sensitivity of the method and certainly the use of oligonucleotides for the tumor specific V(D)J clonal TCR gene rearrangement would be too sensitive. Intriguingly the relative proporitons of their T1/T2 patients with preipheral blood T cell clones are similar to our findings in early stage disease. This suggests that the sensitivity of the two techniques are broadly similar, which would be expected given that both methods depend on distinguishing clonal rearrangements on the basis of sequence and size. In fact our method employed monoplex rather than multiplex polymerase chain reaction and radioactively labelled products which should increase the sensitivity. There is certainly no basis for the authors contention that our approach is less sensitive but comparative studies would be worthwhile.

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The study by Laetsch *et al* has reveaeled similar findings to our study, namely that almost 75% of CTCL patients with stage III–IVb disease have peripheral blood T cell clones. The essential aspect of this study is that both the presence of a peripheral blood T cell clone and the CD4+/CD7-cell count are independently correlated with stage. They have not drawn any conclusions regarding the prognostic significance of their data as suggested by Muche *et al*.

Finally Muche *et al* speculate about physiologic recirculation of tumor cells. We agree that tumor cells will recirculate physiologically but the detection of these cells can still represent a measure of tumor burden and these two concepts are not mutually exclusive.

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REFERENCES

Fraser-Andrews E, Woolford A, Russell Jones, R, Seed PT, Whittaker SJ: Detection of a peripheral blood T cell clone is an independent prognostic marker in mycosis fungoides. *J Invest Dermatol* 114:117–121, 2000

Muche M, Lukowsky A, Alnhudt C, Gellrich S, Sterry W: Peripheral blood T cell clonality in mycosis fungoides–an independent prognostic marker? *J Invest Dermatol* 115:504–505, 2000